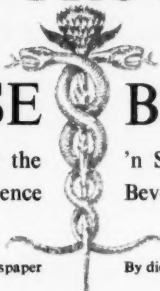


MEDICAL PROCEEDINGS

MEDIESE BYDRAES

A South African Journal for the
Advancement of Medical Science

'n Suid-Afrikaanse Tydskrif vir die
Bevordering van die geneeskunde



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Preparate en Toestelle · Preparations and Appliances · Correspondence

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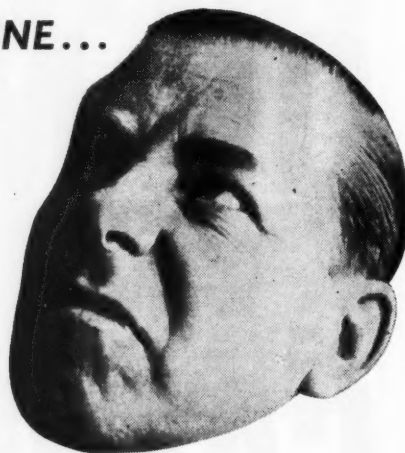
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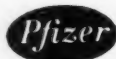
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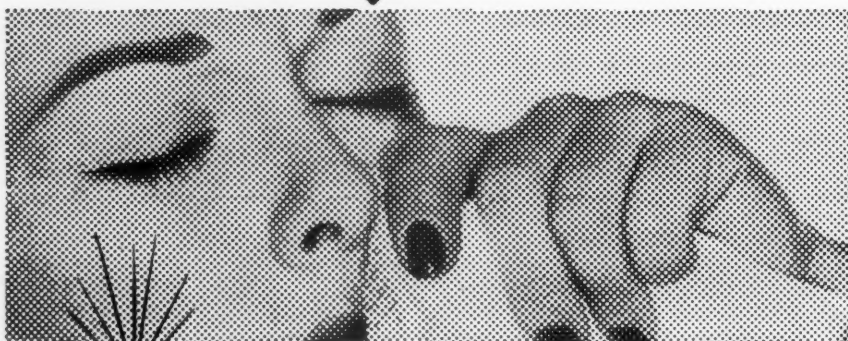
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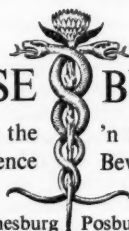
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Vol. 2

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No. 11

REDAKSIONEEL · EDITORIAL

NOVOBIOSIEN

KLINIESE VERSLAE

In 'n vorige uitgawe van hierdie Tydskrif¹ het ons die aandag gevestig op die ontdekking van 'n nuwe antibiotikum wat deur *Streptomyces niveus* of *spheroides* geproduseer word en die algemene naam *novobiosien*² dra. Ons het ook daarop gewys dat die basiese inligting wat reeds ingewin is, kliniese proefnemings met hierdie nuwe chemoterapeutiese middel regverdig.

Die eerste gepubliseerde kliniese verslae is tans beskikbaar. 'n Volledige uitgawe van *Antibiotic Medicine*³ is aan die kliniese waarde daarvan gewy. Uit hierdie gegewens blyk duidelik dat hierdie antibiotikum bes moontlik eersdaags 'n definitiewe plek in ons terapeutiese wapenrusting kan inneem.

Die getuienis dui daarop dat novobiosien 'n besonder kragtige antibiotikum met 'n betreklik breë antimikrobe-spektrum is. Dit het die veelvuldigheid en omvang van sekere chirurgiese prosedures by die behandeling van

NOVOBIOCIN

CLINICAL REPORTS

In a previous issue of this Journal,¹ we drew attention to the discovery of a new antibiotic produced by *Streptomyces niveus* or *spheroides* and known generally as *novobiocin*.² We also pointed out that the basic information gathered justified a clinical trial of this new chemotherapeutic agent.

The first published clinical reports have now become available. A complete issue of *Antibiotic Medicine*³ has been devoted to its clinical value. From these data it is quite clear that this antibiotic may find a definite place in our therapeutic arsenal.

The evidence is that novobiocin is a highly potent antibiotic with a fairly wide antimicrobial spectrum. It has reduced the incidence and magnitude of certain surgical procedures in the treatment of infections of soft tissues, and has been used as a most effective antibiotic in the treatment of staphylococcal infections, since staphylococcal strains that strongly

1. Redaksioneel (1956): Hierdie Tydskrif, **2**, 271.
2. Bekend as *Albamycin* (Upjohn), *Cardelmycin* (Pfizer) en *Cathomycin-kapsules* (Merck).
3. *Antibiotic Medicine* (1956): **2**, Nr. 4, bl. 201-289. New York: MD Publications, Inc., 30 East 60th Street.

1. Editorial (1956): This Journal, **2**, 271.
2. Known as *Albamycin* (Upjohn), *Cardelmycin* (Pfizer) and *Cathomycin Capsules* (Merck).
3. *Antibiotic Medicine* (1956): **2**, No. 4, pp. 201-289. New York: MD Publications, Inc., 30 East 60th Street.

infeksies van die sagte weefsels verminder, en is gebruik as 'n uiters doeltreffende antibiotikum by die behandeling van stafilococcus-infeksies, want daar is bevind dat stafilococcus-soorte wat kwaai weerstand bied teen al die gewone antibiotica wat in hospitale gebruik word, voor novobiosien swig. Dit word dus aangedui vir die behandeling van wondinfeksies ná 'n operasie, weefselontsteking, stafilococcus-septisemie, spatarsweere, terugkerende en hardnekkige pitsweere, verskillende vel-absesse, ingewandsonsteking en paronichie. Daar word berig dat novobiosien ook voor-trefflike resultate opgelewer het by die behandeling van infeksies wat deur die vatbare *Proteus*-soorte veroorsaak is. Die nuwe antibiotikum het die bewys gelever dat dit hoogs doelmatig is vir die uitroering van 'n aantal ander organismes soos streptococcus, diplococcus, corynebacterium en *Pasteurella*. Verdere inligting oor hierdie saak sal met verloop van tyd beskikbaar gestel word. Klinies is daar nog nie bewys dat dit 'n amebedoder is nie.

Novobiosien is 'n doeltreffende antibiotikum vir sekere pasiënte wat allergies is vir die mikrobebestrydende middels wat gewoonlik gebruik word, en geen moniliale superinfeksie is gerapporteer nie.

Geen kruisweerstand is waargeneem tussen novobiosien en ander antibiotica nie, en dit het 'n sinergistiese bakteriedodende effek met penisillien, chlortetrasiklien, oksitetrasiklien, chloramfenikol, streptomisien, baksitrasien, neomisien, streptotrisien en grisein, soos gedemonstreer *in vitro*.

Die toksiese en die sensitiwiteitseffek is nie opvallend nie, maar daar is bewyse dat die mondelinge toediening daarvan aanleiding kan gee tot netelroos of macula-papuleuse huidontsteking. Die voorkoms van hierdie velreaksies by pasiënte wat 'n daaglikse dosis van 1.0 g. ontvang, is 0.5%.

Die middel is bakteriedodend teen omtrent twee keer die minimale inhibisie-konsentrasie. Aansienlike en standhoudende bloedpeile word verkry volgende op die mondelinge toediening daarvan.

Die hoë konsentrasie in die serum moet miskien toegeskryf word aan die her-absorpsie van die antibiotikum uit die derm, want groot hoeveelhede daarvan word in die gal afgeskei. Die suggestie dat dit miskien liggies deur serumproteïene gebind word, bring waarskynlik die moontlikheid mee dat dit 'n reservoir kan word vir latere vrystelling in die bloedsomloop.

Daar is getuigenis dat sommige bakterieë weerstand teen novobiosien sal opbou, en dit beklemtoon die noodsaaklikheid om te waak teen die onoor-deelkundige en ongeoorloofde gebruik van antibiotica in die algemeen.

Verdere kliniese verslae sal die rol wat hierdie belangrike nuwe antibiotikum in die behandeling van infeksies kan speel, ongetwyfeld duideliker definieer, maar die algemene mening skyn te wees dat die voorlopige kliniese ondervinding met novobiosien bemoedigend is.

resist all the commonly employed antibiotics, as frequently occur in hospitals, respond to novobiocin. It is thus indicated for the treatment of post-operative wound infections, cellulitis, staphylococcal septicaemia, varicose ulcers, recurrent and persistent carbuncles, various skin abscesses, enteritis, and paronychia. Novobiocin has also been reported to produce excellent results in the treatment of infections due to susceptible strains of *Proteus*. This new antibiotic also has demonstrated a high degree of efficacy in eradicating a number of other organisms, such as *Streptococcus*, *Diplococcus*, *Corynebacterium* and *Pasteurella*; further information on these uses will be forthcoming. It is not clinically established as an amoebicidal agent.

Novobiocin is an effective antibiotic for certain patients allergic to the commonly used antimicrobials, and no monilia superinfection has been reported.

No cross resistance has been observed between novobiocin and other antibiotics, and it has synergistic bactericidal action with penicillin, chlortetracycline, oxytetracycline, chloramphenicol, streptomycin, bacitracin, neomycin, streptothricin, and grisein, as demonstrated *in vitro*.

Toxic and sensitivity effects were not conspicuous, but evidence has emerged that oral administration may give rise to urticaria or maculopapular dermatitis. The incidence of these skin reactions in patients receiving daily doses of 1.0 g. is 0.5%.

The drug is bactericidal at about twice the minimal inhibitory concentration. Very considerable and persistent blood levels are obtained following oral use.

The high concentration in the serum may be due to reabsorption of the antibiotic from the gut, since it is excreted in large quantities in the bile. The suggestion that it may be loosely bound by serum proteins may enable it to provide a reservoir for subsequent release into the circulation.

There is evidence that some bacteria may develop resistance to novobiocin and this emphasizes the need to observe the principle of avoiding indiscriminate or unwarranted use of antibiotics generally.

Further clinical reports will undoubtedly define more precisely the role of this important new antibiotic in the treatment of infections, but the general consensus of opinion seems to be that clinical experience to date with novobiocin is encouraging.

GENADE-DOODSLAG

R. P. DAVIDOW

Joseph Davidow, 26 jaar oud, is aangekla van die moord op sy moeder. Hy het haar dood-geskiet omdat hy nie langer haar lyding kon aanskou nie.

Soos reeds bekend, is Davidow onskuldig bevind en ontslaan. Om die aanklag van moord te staaf, was dit nodig vir die Kroon om drie dinge te bewys: dat iemand om die lewe gebring is, dat die doodslag onwettig was, en dat die doodslag gepleeg is met die doel om te vermoor. Die verdediging het beweer dat daar geen bedoeling was om doodslag te pleeg nie; of, as alternatief, dat as daar wel so 'n bedoeling was, daardie bedoeling hom geopenbaar het gedurende 'n emosioneel versteurde tydperk toe die beskuldige die slag-offer van 'n onweerstaanbare drang was.

Die mediese getuienis was van die aller-grootste belang, en die hele saak het uitsluitend gewentel om die deskundige getuienis wat deur mediese praktisyns afgelê is. Die deskundige van die Kroon het die mening uitgespreek dat die beskuldige histeries was en outomaties opgetree het ten tyde van die doodslag. Ten gevolge van die ernstige spanning waaraan die beskuldige oor 'n lang tydperk blootgestel was, het iets binne in hom 'gebreek', en sy latere dade was outomaties en sonder bedoeling. Wat hierdie punt betref, het die psigiaters van die Kroon en die verdediging saamgestem dat die beskuldige nie bedoel het om te moor toe hy die noodlottige skoot afgevuur het nie. Na aanleiding hiervan het die regter voor wie die saak gedien het die opmerking gemaak dat die saak teen die beskuldige feitlik teruggetrek is deur die Kroon. Hy het derhalwe opdrag aan die jurie gegee om die beskuldige onskuldig te bevind. Volgens 'n koerantverslag* het die regter ook aan die juriesede gesê dat as hulle die mediese getuienis wat afgelê is, nie kon volg nie, dit hom glad nie sal verbaas nie. Dit verbaas ons ook nie. Die regter se vrae aan kroongetuies het aan die lig gebring dat daar inderdaad getuienis was van 'n regsbedoeling om dood te maak (briewe, gesprekke en ander gedrag oor 'n tydperk van 2 jaar, in die loop waarvan die beskuldige sy voorneme om sy moeder om die lewe te bring, aangekondig het). Hoewel die hof 'n behoorlike en bevoegde uitspraak gegee het op grond van die getuienis wat aan hom voorgelê is, kan daar wel betwyfel word of die uitspraak korrek was.

* *Rand Daily Mail*, 21 Junie 1956.

MERCY KILLING

R. P. DAVIDOW

Joseph Davidow, aged 26, was charged with the murder of his mother whom he shot because he could no longer bear to see her suffering.

As is now well known, Davidow was found not guilty and acquitted. To establish murder, it was necessary for the Crown to prove three things: that there was a killing, that the killing was unlawful and that the killing was done with the intent to kill. The Defence alleged that there was no intention to kill; alternatively, if there was such an intention, the intention operated during an emotionally disturbed period when the accused was the victim of an irresistible impulse.

The medical evidence was crucial and the whole case turned exclusively on the expert testimony given by medical practitioners. The Crown expert took the view that the accused was hysterical and acted automatically at the time of the killing. As a result of severe strain over a prolonged period, 'something snapped' in the accused's mind and his subsequent action was automatic and without intent. In the event, the Crown and the Defence psychiatrists were in agreement that the accused had no intention to kill when the fatal shot was fired. This led the presiding judge to remark that the case against the accused had virtually been withdrawn by the Crown. He therefore directed the jury to find the accused 'not guilty'. According to a newspaper report,* the judge also remarked to the jury that if they could not follow the medical evidence which had been led, he would not be surprised; nor would we. The judge's questions to Crown witnesses indicated that there was, in fact, evidence of a legal intention to kill (letters, conversations, and other conduct over a period of 2 years in the course of which the accused announced his intention to kill his mother). Although the Court found a proper and competent verdict on the evidence before it, it may well be disputed whether the verdict was correct.

The Court is never tied by expert evidence, which it may discard because it lacks cogency. In view of the premeditation, there must be great difficulty in understanding how the behaviour of the accused was either automatic or the result of an irresistible impulse. The word 'impulse' means what is says and there was clearly considerable premeditation. More-

* *Rand Daily Mail*, 21 June 1956.

Die hof laat hom nie bind deur deskundige getuënis nie, en kan dit verwerp as dit geen bewyskrag het nie. Met die oog op die voorbedagtheid is dit nogal moeilik om te begryp hoe die gedrag van die beskuldigde of as outomaties of as die gevolg van 'n onweerstaanbare drang bestempel kon word. Die woord 'drang' beteken presies wat dit sê, en daar was heel duidelik aansienlike voorbedagtheid. Temeer, moorddadige dade voortspruitende uit 'n onweerstaanbare drang, geassosieer met 'n psigo-neurotiese obsessie-kompulsiewe toestand, is seldsame verskynsels—as hulle geheel en al voorkom. Geen duidelike en definitiewe psigiatriese diagnose is met eensgesindheid in hierdie saak vasgestel nie. Oor die kwessie van onweerstaanbare drang val daar by hierdie geleentheid dus te redeneer.

Ons hoë reeds beslis dat 'n daad wat in blinde woede gepleeg word, nie 'n onweerstaanbare drang (as verdediging teen 'n moordaanklag) is nie. In die omstandighede van die Davidow-saak word die frase 'onweerstaanbare drang' feitlik van sy duidelike betekenis beroof, tensy ons so 'n bietjie ekstra aan ons woorde betaal om 'n ietsie meer vir ons te beteken.

'n Ander punt wat duidelik geblyk het uit hierdie verhoor is die groot kloof tussen die regs- en die psigiatriese begrippe van bedoeling en beheer oor die emosies. Op hierdie gebied is dit duidelik dat advokate en geneesherse eenvoudig nie dieselfde taal praat nie; en, wat hierdie probleem betref, betwyfel ons of daar selfs gesê kan word dat dokters onderling dieselfde taal praat. Dit manier waarop daar geredeneer is oor outomatisme en onweerstaanbare drang laat ons dink aan 'n psigiatriese Toring van Babel liewer as aan die presiese taal van die wetenskap.

En punt moet beklemtoon word. Die uitspraak in hierdie besondere saak dien nie as regverdiging vir genade-doodslag nie. Inderdaad het die saak geen betrekking op en staan hoegenaamd nie in verband met die probleem van eutanase nie, want daar is bevind dat die beskuldigde opgetree het sonder die regsbedoeling om doodslag te pleeg. Hy is vrygespreek weens die aard van die mediese getuënis wat die saak finaal beslis het. Sonder hierdie getuënis sou die beskuldigde ongetwyfeld skuldig aan moord bevind gewees het, maar waarskynlik met versagende omstandighede. (Trouens, in Engeland is die argument van onweerstaanbare drang geen verdediging in geval van 'n moordaanklag nie.)

Dit is die tweede onlangse geval waar outomatiese gedrag 'n beskuldigde geëls het in 'n moordverhoor. In albei gevalle is die uitspraak miskien 'n weerspieëling van 'n sekere mate van openbare simpatie met die beskuldigde, maar mediese kringe is verontus oor hierdie gevalle. Miskien is dit nodig om ons wette te verander sodat die probleem van persone wat emosioneel abnormaal en tog intellektueel ongeskonde is, hoewel hul redeneervermoë tydelik miskien oorweldig is, die hoof gebied kan word; maar hierdie soort hervorming is iets wat by die parlement liewer as by die hof tuis behoort.

Die probleem, soos ons dit sien, is besonder moeilik in teorie sowel as in praktyk; en tog twyfel ons nie daaraan nie dat daar andere is vir wie die saak die eenvoud self is.

over, homicidal acts resulting from an irresistible impulse associated with a psychoneurotic obsessive-compulsive state must be extremely rare, if they occur at all. No clear and definite psychiatric diagnosis was established with unanimity in this case. The issue of an irresistible impulse is therefore a very arguable one on this occasion.

Our Courts have held that an act done in a blind rage does not constitute an irresistible impulse (as a defence against murder). In the circumstances of the Davidow case, the phrase 'irresistible impulse' is virtually shorn of its clear meaning unless we pay our words extra to mean something more.

Another point which emerges clearly from this trial is the great gap between the legal and the psychiatric concepts of intention and the control of the emotions. In this field, lawyers and doctors clearly do not speak the same language; and we doubt whether even doctors can be said to speak the same language amongst themselves in this kind of problem. The manner in which automatism and irresistible impulse have been debated, suggests a psychiatric tower of Babel rather than the precise language of science.

One point must be emphasized. The outcome of this case does not condone mercy killing. Indeed, the case has no bearing on and is unrelated to the problems of euthanasia because the accused was held to have acted without a legal intention to kill. He was acquitted because of the nature of the medical evidence, which decided the issue conclusively. Without this evidence, the accused would undoubtedly have been found guilty of murder, though probably with extenuating circumstances. (Indeed, in England the argument of an irresistible impulse is no defence to a charge of murder.)

This is the second recent occasion on which automatic behaviour has availed an accused person successfully when facing a capital charge. The verdict in each case may reflect a certain public sympathy with the accused, but medical circles have undoubtedly been disturbed by these cases. There may well be a need for changes in our law to cope with the problems of those who are emotionally abnormal yet intellectually intact, though their reasoning powers may temporarily have been overwhelmed; but this kind of reform is a matter for Parliament rather than the Courts.

The problem is, as far as we can see, an extremely difficult one, both in theory and in practice; yet we do not doubt that there are others for whom the situation simply bristles with simplicity.

VASCULAR SURGERY

THE PRESENT POSITION*

A. LEE MCGREGOR, CH.M. (EDIN.), F.R.C.S. (ENG.)†

Johannesburg

In 1877 Eck established communication between the portal vein and the vena cava experimentally. Having thus made history, he disappeared into the army. Fifty years later Eliakim of New York successfully applied the lessons of the laboratory to human beings. In 1902 Carrel had shown that arteries could be successfully joined—the essence of his success being asepsis and the avoidance of stricture by triangulating the vessel. Half a century lapsed once again before this laboratory exercise was to become of value to ailing humanity. Once begun, however, the surgery of the vascular system advanced with great rapidity and to-day scientific journals bulge with accounts of this work.

The surgery of the blood vessels as now practised is one of the great events in the long history of surgery. The object of this paper is to acquaint my surgical colleagues of my impressions of a recent visit to Professor Rob's vascular clinic at St. Mary's Hospital, London, in December 1955. Of greater import, however, is to bring to the notice of the profession as a whole, the great strides that have been made in the surgery of the blood vessels. The great majority of doctors are in country areas where they have neither the time to study nor access to the literature dealing with such matters, and if we are to do justice to our patients with surgical diseases of the blood vessels, it is necessary to know something about prognosis and of what modern methods can achieve. The treatment of obliterative diseases of the blood vessels, and particularly of athero- and arteriosclerosis, is surgical. To waste valuable time by the exhibition of vasodilators, venous occlusion, tocopherols, etc. (all largely discredited) is not only to lull oneself and the sick public into false security, but also to do actual harm by allowing the time for successful surgery to slip by. Medicine

has an important part to play in the handling of vascular lesions, but it is in the field of prevention. Once the blood supply to a limb is diminished, it is only the surgeon who can help.

PROGRESS ABROAD

PORTAL HYPERTENSION

In 1948 I had the privilege of seeing the work being done on cirrhosis of the liver by venous shunts in New York, Copenhagen, Stockholm and London. It was immediately obvious that this immensely difficult work was not 'everybody's job'. Not only did it require surgical skill of the highest order, but also a large team including physicians, biochemists, anaesthetists, specially trained nursing staff, etc. It was therefore not justifiable to undertake this work unless these desiderata could be complied with. In those years also Crafoord, Gross, Hufnagel and others were becoming familiar with division and suture of the aorta and the closing of the patent ductus arteriosus.

In 1950 Mr. Pieter Theron, F.R.C.S. (Eng.), became first assistant to Professor Underwood in the Department of Surgery at the University of the Witwatersrand. With his experience and special training, and with the facilities of a large hospital at his disposal, he was able to embark on the surgery of portal hypertension with notable success in a fair series of cases. I understand that Mr. Theron is preparing this work for publication. It is to be deplored that the economic bleakness which seems to be a *sine qua non* of all Government or Provincial medical and surgical appointments, has driven so fine a worker from the academic atmosphere which he loved and adorned.

The surgery of portal hypertension is now established on a firm basis. Some workers such as Linton consider that spleno-renal shunts are, when feasible, the more advisable in portal hypertension. I saw 2 successful porto-caval shunts in Professor Rob's wards at St. Mary's, recently. In both cases there was a

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large splenic vein present. In response to my query Professor Rob informed me that in cases of intra-hepatic block he preferred to perform end-to-side porto-caval anastomosis.

THROMBO-ENDARTERITIS

SYMPATHETIC DENERVATION

In South Africa we see a great many cases of chronic arteritis, mainly of arteriosclerotic origin, and affecting the abdominal aorta or its branches. In many such cases, provided the

THROMBO-ENDARTERECTOMY

For many years the operation of embolectomy had been practised with such indifferent success that even now many authorities are doubtful of its value. This applies to emboli of recent lodgement. Of latter years, however, surgeons have become more aggressive and the aorta and its branches have been opened to remove organized thrombi obstructing the aortic bifurcation or its larger branches (Fig. 1).

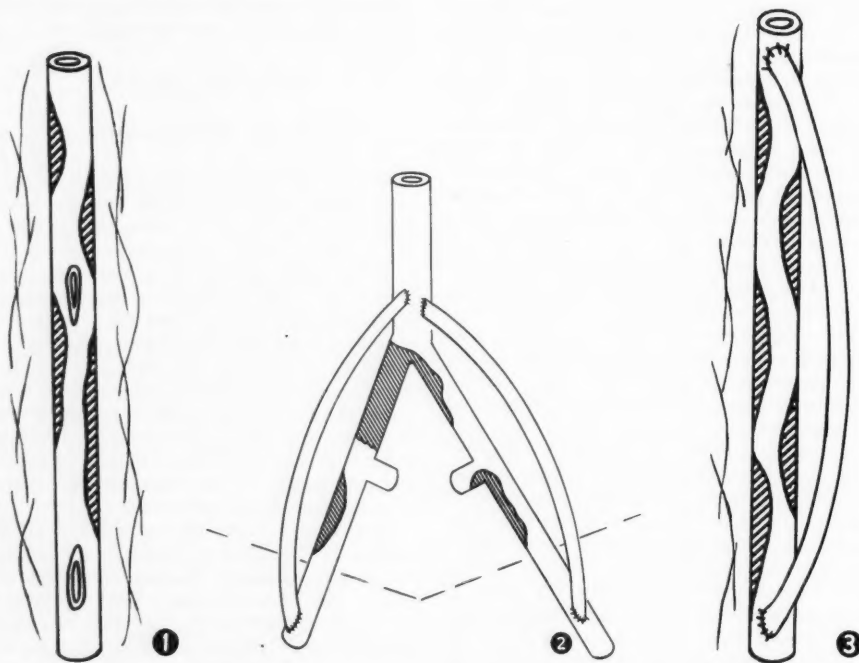


Fig. 1. Diagrammatic representation of an atherosclerotic blood vessel. Two openings have been made in the vessel to remove the organized thrombi. These openings are subsequently closed. The collateral circulation round the partly obstructed vessel is indicated.
Fig. 2. This shows diagrammatically the organized thrombi in the iliac vessels of the patient just described. On either side a by-pass human graft connects the aorta to the common femoral artery. This is the operation which would have been preferable in this patient.

Fig. 3. A diagram of a partly obliterative artery showing a by-pass human graft inserted by the end-to-side method.

existence of active vasoconstriction can be demonstrated pre-operatively, much help can be given to the patient by sympathetic denervation, and perhaps half of those suffering from exercise pain are able to walk better. The operation is valuable, has no mortality and continues to be widely practised.

Many glowing accounts of the success of thrombo-endarterectomy have been published. The procedure conflicts with one's ideas of the physiology of intravascular clotting. The attack is made on a vessel which suffers from a generalized disease of the blood vessels. More or less violence inflicts unavoidable

trauma on the inner surface of the artery, so that the prospects of the re-establishment of a healthy intima and a continued unimpeded blood flow are not good. We have satisfied ourselves from our own endeavours in this type of work that, whereas some thrombi will ream out with ease, leaving a relatively undamaged medial coat, others can only be removed by the exercise of such trauma that disaster is unavoidable. Probably all surgeons carrying out thrombo-endarterectomy are harried by similar fears and experiences.

Mr. H., a road overseer aged 60, was unable to do his work because of increasing tiredness of his right lower limb, hip and buttock areas. He was otherwise well. The condition of his lower limbs was as follows:

There were no pulses on the right and those on the left, though present, were feeble. An aortogram done by Dr. Denny (then on the staff of the Radiological Department of the Johannesburg General Hospital) showed a blocked right common iliac artery and a considerable irregular narrowing of the left one. The Wassermann tests were negative and other examinations not noteworthy.

At operation the abdomen was opened by a full-length vertical incision, the small bowel eviscerated, and the aorta and its branches exposed. The right common iliac artery was tortuous and completely blocked. The external iliac was non-pulsatile. The right common femoral artery was exposed and, though also arteriosclerotic, there was a fair blood flow when the vessel was opened. A by-pass human arterial graft was inserted connecting the terminal aorta with the common femoral. There was strong pulsation in the graft. The left common iliac artery was reduced to half its diameter by organized thrombus formation. It was opened and attempts made to remove the obstructing material. This required so much force and inflicted such trauma that it was felt that new thrombi would of necessity form in the vessel. This is just what happened. Although the operation was well tolerated, intravascular clotting took place, spread up the aorta and caused the death of the patient (Fig. 2).

Had the common iliac artery been left alone and a by-pass graft been inserted (as was done on the right side) the patient would have escaped the hazards of endarterectomy.

ARTERIAL GRAFTING

In 1954 I had the privilege of watching Dr. R. Linton (of the Massachusetts General Hospital in Boston) using human arterial grafts in the treatment of arteriosclerotic vessels. The operation then being done was to exclude the narrowed artery by dividing it above and below and joining the upper to the lower ends by a healthy human graft. It is a principle in dealing with arteriosclerotic vessels, that they are interfered with as little as possible so that the important collateral circulation is not impaired. An exception is made in the case of the aortic bifurcation where this is removed, as

there is no room for the damaged vessel and the graft.

Dr. Linton was putting in grafts from the inguinal ligament to the popliteal artery and later from the aorta below the renals to the popliteal on both sides. The surgery was indeed impressive to the observer, and especially so to the patient, who had been crippled by intermittent claudication and who was able, after surgery, to walk much longer distances.

In a recent communication Dr. Linton tells me that some of these cases have been disappointing as the grafts have become occluded by thrombosis. The reason for this has been stricture followed by clotting at the site of the end-to-end anastomosis. Dr. Linton is now using Cockett's method of end-to-side anastomosis. The essence of the matter is that the narrowed artery is not interfered with at all,¹ except for the making of a vertical slit above and below the area of damage. To these slits are anastomosed the ends of a human arterial graft. In this way the host vessel is not narrowed, the collateral is not disturbed and, should the graft obliterate, there is no harm done. The graft is inserted in a tunnel made in the tissues so that the collateral is not impaired (Fig. 3).

THE OUTLOOK IN OBLITERATIVE VASCULAR DISEASE AFTER GRAFTING

When one considers that arteriosclerosis is a progressive disease which occurs mainly in elderly people, it is not to be wondered at that a considerable proportion of grafting procedures fail. It is remarkable that so many are benefited by the operation. What is important is that the patient should not be made worse by surgery and this is the case with the by-pass graft.

I was much impressed at St. Mary's Hospital in London by the great conservatism exercised by Professor Rob in choosing cases of degenerative vascular disease for surgery. If the patient could get to his job, even though he had exercise pain, he was not operated on. He was helped by raising his heel or improving his walking. Surgery was a final resort. There is great authority for not pouring new wine into old bottles. Cases are recorded of the sufferer's walking power being so much helped by surgery that the unwonted exertion precipitated a coronary lesion!

AORTIC ANEURYSM

Having stressed the fact that conservatism is the keynote of the treatment of occlusive vas-

cular disease of the limb vessels, I must now stress the aggressive nature of the attack on aneurysm of the abdominal aorta.

Eighty per cent of persons suffering from this disease will die from rupture of the aneurysm within 2 years. I have on occasion heard doctors say that they have watched such cases for many years and that the patients have not been any the worse for the waiting. This is not in accordance with the facts. It is even less reasonable than advising the owner of gall stones or gastric ulcer that his interests are better served by avoiding the risks of surgery. Thus in any abdominal aortic aneurysm surgery is advised whether or not it is causing symptoms. Aneurysms have been operated on for many years and the profession as a whole is conversant with the condition and its surgery. Abdominal aneurysm posed a hopeless problem until it was shown that the lesion could be removed and replaced by a human graft or a prosthesis. In 1954 I had the privilege of seeing Dr. Blakemore resect an aortic aneurysm in an old man with a dreadfully damaged arteriosclerotic aorta. He inserted a Vinyon cloth bifurcation graft. The operation took 8 hours. When the clamps were removed there was not the leakage of a drop of blood at any of the 3 sites of arterial anastomosis. Operations of this type are now common surgical practice. It is of pathological interest that aortic aneurysms below the renal arteries are not of syphilitic but of arteriosclerotic origin.

TYPES OF GRAFT

Many materials have been used as grafts. The favoured one has been a human graft from a healthy subject under 30 years old. Such material is scarce everywhere, and although special legislation has been enacted in the Union for procuring it, the provisions are cumbersome and often impracticable. Moreover, collection, preparation and storage present many problems. Most surgeons have agreed that human grafts will be replaced by plastic ones.

A satisfactory prosthesis should be in free supply, present no storage or sterilization problems, and be generally available. Nylon, sturgynol, and other materials have been used. The ends had to be turned back to hold a suture so that sewing the graft in place was difficult. Mr. Eastcott pointed out to me that to prevent weakness and sheering stresses at the junction of the graft with the host vessel, the prosthesis would need to be elastic, which

nylon is not. It has been abandoned as a vascular conduit at St. Mary's Hospital.

POLYVYNIL PROSTHESIS

When I visited St. Mary's Hospital, Paddington, in December, Professor Charles Rob had been using polyvynil for a sufficiently long period to feel that it represented a great advance in arterial surgery. He was using it for aortic bifurcation grafts as a routine and also in the limbs. He was not yet sure that tubes made of this material would be satisfactory across limb flexures, but he used it to replace defects in vessels after excision of popliteal aneurysms, so I gather he is moderately satisfied on this score. Experimental work is in progress all the time. On one occasion Professor Rob was good enough to take me to the Royal Veterinary Hospital where a polyvynil tube was made on the spot and inserted in the femoral artery in the groin of a greyhound. The dog was subsequently moved to a country establishment where field exercise exposed the prosthesis to the tests necessary to determine the effects of flexion on the plastic. Mr. Owen, Professor Rob's first assistant, informed me that the material was being subjected in specially designed machines to strains similar to those sustained in the human body during the course of a lifetime. The machine could achieve this result in a comparatively short period. Thus the search for the perfect prosthesis is continuing unabatedly.

MAKING THE PROSTHESIS

I had the privilege of watching Professor Rob or his team insert polyvynil prostheses in the aorta and the limb vessels. The material is used, I believe, for many purposes in industry, such as padding for motor-car seats. It is delivered in the form of an ordinary builder's brick. It is white, very light, fairly hard and looks much like a sponge, being riddled with holes of various sizes. It is cut into slices about 2 mm. thick. These in turn are sliced by scissors to a width of about 1 inch. The material is thus prepared for use in the theatre (Fig. 4).

From the aortogram the surgeon assesses the length and bore of the graft. A number of metal moulds is available. They are made by the hospital engineer in the form of the vessel needing replacement. If an abdominal aneurysm has been exposed, the assistant notes the size of the bifurcation prosthesis

which will be needed. He chooses the requisite mould and round this he winds the polyvinyl strips to the length and thickness neces-

in a tuberculous abscess cavity without being influenced by the infection.

The other important characteristic of the graft is its elasticity, which is comparable to that of the host artery, thus obviating any sheering stress at the junctional areas. Furthermore, it has no weak areas such as a human graft presents in situations where its branches have had to be ligated, or where the intima has been damaged.

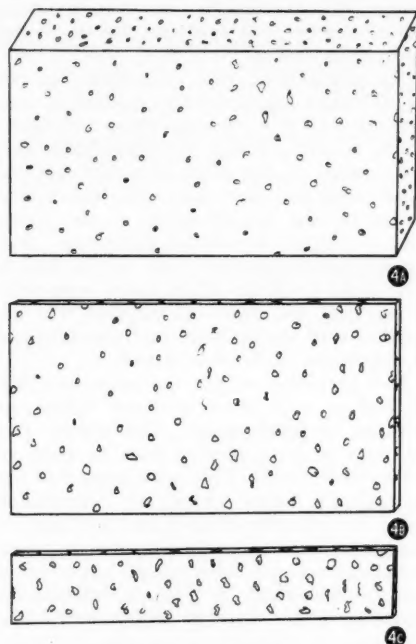


Fig. 4. This shows a polyvinyl brick (A). In (B) a slice has been cut off the brick. In (C) a portion of this slice which is ready for winding on the prosthesis.

sary. The strips are held in place by a narrow bandage. The apparatus is then boiled for 20 minutes (Fig. 5).

On removal from the sterilizer it is handed to the surgeon. The bandage is taken off and the mould removed by unscrewing its component parts and pulling them out of the graft. The prosthesis now looks much like a portion of a bicycle tyre tube except that it is greyish in colour. The inner surface is shiny, smooth and homogeneous. The outer surface has a porous appearance. It is elastic and compressible and can be cross clamped without being injured. It transmits a needle easily. The inner surface is so smooth that it offers no opportunity for blood to clot and the porosity of the outer surface is ideal for the ingrowth of granulation tissue to form a sheath for the graft. It is not absorbed, as most of the human graft is, and it is resistant to infection. This was well demonstrated where such a graft lay

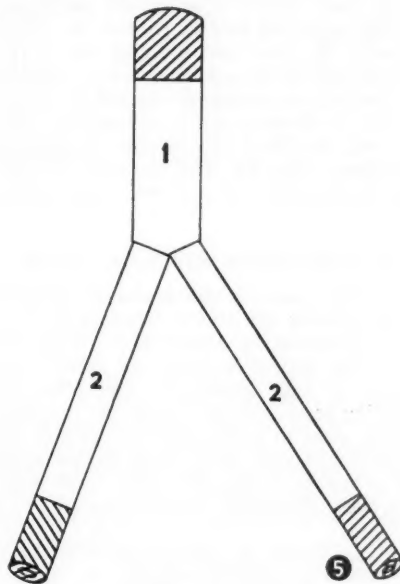


Fig. 5. This represents a metal mould for an aortic bifurcation graft. The ends of the mould are gnurled. After the graft has been made the limbs (marked 2 in this Figure) are unscrewed from it and pulled out of the prosthesis. Part 1 of the mould is then pulled out.

INSERTING THE PROSTHESIS

The aneurysm having been removed by division of the aorta above and the common iliac arteries below, the suitable graft is cut squarely across at one end and laid in apposition with the host artery—in this case the divided aorta below the renals and is sutured to this vessel. The nature of the material is such that it does not admit of eversion such as homografts or the nylon group of materials do. In inserting polyvinyl, end-to-end apposition is aimed at. Thus instead of a complicated type of suturing all that is necessary is a simple over-and-over

suture. As the insertion of the suture in a deep recess may be a very difficult matter, the word simple as used here must not be misconstrued. In the insertion of homografts some tension is advisable on the graft. None is needed in applying plastic grafts. When the 3 lines of suture of the bifurcation graft have been inserted, the lower clamps (on the iliac arteries) are removed and then the one on the abdominal aorta. In the cases I saw done there was quite brisk haemorrhage at all 3 suture lines. Swabs were packed round the bleeding areas and held in position for 15-20 minutes. By this time bleeding was much reduced and by the use of sufficient patience the bleeding was ultimately controlled. In no case was it alarming and it is surprising how little was the blood loss in these formidable procedures. The day after operation patients were surprisingly well and were soon ambulatory.

ANEURYSMS ABOVE THE RENAL VESSEL

These carry a grave prognosis and are operated on by reducing the patient's temperature in a cool atmosphere by numerous ice bags and fans. The danger is renal and spinal cord anoxia by the prolonged application of occluding aortic clamps. It may be necessary in such cases to detach a vessel such as the superior mesenteric artery from the aneurysm and re-implant it into the graft. Such cases have been successfully operated on.

THE POSITION OF ARTERIAL SURGERY IN SOUTH AFRICA

Surgeons in this country have attained considerable experience in the type of vascular lesion consequent on trauma. The wars and Native brawls have supplied material for the surgery of traumatic aneurysms, arterio-venous fistulae, etc. It is to be hoped that these experiences will be placed on record. We are just entering the field of arterial replacement and throughout the country surgeons are avid to embark on this work. This has meant an immense amount of planning and organization. I can speak only of what has happened in Johannesburg, though similar work advances apace elsewhere in the country. In the Department of Surgery of the University of the Witwatersrand, under the direction of Prof. W. Underwood, a great deal of work has been and is being done in the sphere of cardiac and vascular surgery. There is a well established, fully equipped section dealing with all phases of the 'up to the moment' surgery of the

heart and the great vessels.

The Radiological Department at the Johannesburg General Hospital, under the direction of Dr. Josse Kaye, has great experience in the science of arteriography and has produced special and original apparatus for displaying the vascular system.

The path is beset with great difficulties. In the first place legislation for acquiring human grafts is not yet in the stage where such grafts can be readily procured. Our legislators need to be aware of the elementary fact that the blood vessel of a dead man, quite valueless to its owner, may be life-saving to the person who is crippled by arterial misfortune. Fortunately plastic prostheses are on the way to solving the problem. Then, again, team work is necessary and above all surgeons who are familiar with the problems and the technique of the surgery of the blood vessels.

It is impossible to gain experience and skill in dealing with these problems unless the material is forthcoming. This means that members of the profession must be aware of what can be done. They must learn that just as neglected breast conditions, hypertension and a host of other diseases lead to disaster if not properly treated at the proper time, so too the diseases of the blood vessels can often be successfully treated if they are referred for investigation and possible surgery before it is too late.

I have endeavoured to establish the following principles:

1. The surgery of the blood vessels has become established on a firm basis of fact and experience.

2. It is one of the notable advances in the field of practical medicine of recent years.

3. The treatment of occlusive vascular disease is essentially conservative. Surgery only has a place when non-surgical methods have failed.

4. The surgery of aneurysm is aggressive and holds out great promise to the sufferer.

5. Plastic prostheses are a valuable addition to the surgeon's armamentarium and bid fair to replace human grafts.

6. All work of these types can be done in the Union.

7. No work of these types can be done unless it is referred to centres equipped to deal with such problems.

OPSOMMING

1. Chirurgie van die bloedvate is vandag op die stewige grondslag van feite en ondervinding gegrondevs.

2. Dit is een van die belangrike vorderings wat in die afgelope paar jaar op die gebied van praktiese geneeskunde gemaak is.

3. Die behandeling van okklusiewe vaskulêre kwale is essensieel konserwatief. Chirurgie kry alleen 'n plek as nie-chirurgiese metodes misluk het.

4. Die chirurgie van aneurisma is aggressief, en hou groot belofte vir die slagoffer in.

5. Plastiese prostheses is 'n waardevolle byvoegsel tot die chirurg se wapenrusting, en daar bestaan 'n redelike moontlikheid dat hulle menslike inplantings sal vervang.

6. Al die werk wat onder hierdie tipes ressorteer, kan in die Unie gedoen word.

7. Geen werk van hierdie aard kan egter gedoen

word nie tensy dit verwys word na sentrums wat spesiaal toegerus is om sodanige probleme die hoof te bied.

I wish to place on record my gratitude to Professor Rob of St. Mary's Hospital, London, Dr. A. Blake-more of the Presbyterian Hospital, New York, Dr. Linton of the Massachusetts General Hospital, Boston, and others for their great help and enthusiastic co-operation in giving me all the assistance and advice that I asked for.

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SWELLINGS OF THE NECK

MIDLINE SWELLINGS

JAN H. LOUW, CH.M.*

and

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(Continued from p. 332)

2. *Swellings in the Skin and Subcutaneous Tissues.* Any swelling of the skin or subcutaneous tissues may happen to occupy the midline of the neck. Examples which we have encountered include the following:

(a) *Haematoma* (Figs. 24A, 24B). A boy aged 8 years complained of a painful swelling

below his chin. He had been kicked in this region 4 days before. Examination revealed a midline swelling occupying the whole of the submental triangle. It was firm, with a smooth surface, ill-defined edges and limited to the subcutaneous tissues. The overlying skin was bruised. It gradually disappeared with conservative management.

(b) *Abscess* (Fig. 25). An infant aged 4 weeks presented with a midline swelling in

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Figs. 24A, 24B. Haematoma of the submental region. Note the abrasion of the lip.



Fig. 25 (Left). Metastatic staphylococcal abscess in an infant.

Fig. 26 (Right). Tuberculous suprasternal glands with secondary infection.

the suprasternal region. This had all the features of an acute pyogenic abscess. The diagnosis of staphylococcal metastatic abscess was confirmed by culture of the pus which was evacuated from the swelling.

In Fig. 26 a similar abscess due to mixed tuberculous and pyogenic infection is illustrated.

(c) *Neoplasms.* We have had examples of keloid (Fig. 27), neurilemmoma (Fig. 28), neurofibroma (Figs. 29A, B) and primary malignant melanoma (Fig. 30) which have presented as midline or paramedian swellings

of the neck. The usual clinical features rendered their diagnosis straightforward, although the neurofibroma was at first mistaken for a thyroid adenoma.

(d) *Sebaceous Cyst* (Figs. 31 and 32). Although sebaceous cysts are not often midline, we have had no less than 3 such examples which on casual inspection simulated thyroglossal cysts. The doughy consistency, adherence to the skin and the presence of a punctum served to render the diagnosis obvious.

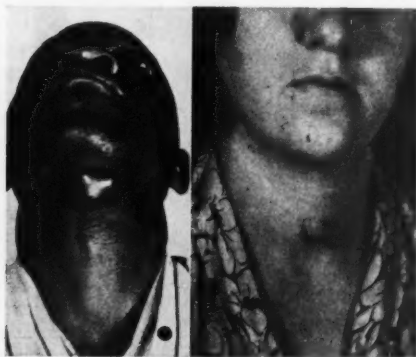


Fig. 27 (Left). Keloid formation in the submental region.

Fig. 28 (Right). Neurilemmoma in the midline of the neck producing a hard fibrous tumour.



Fig. 30. Fungating primary malignant melanoma.

Supplement to Medical Proceedings · Mediese Bydraes, 18 August 1956 Augustus 18

An Important Therapeutic Message

'n Belangrike Terapeutise Boodskap

R_k

*in non-specific rheumatic disorders
in nie-spesifieke rumatiese toestande*

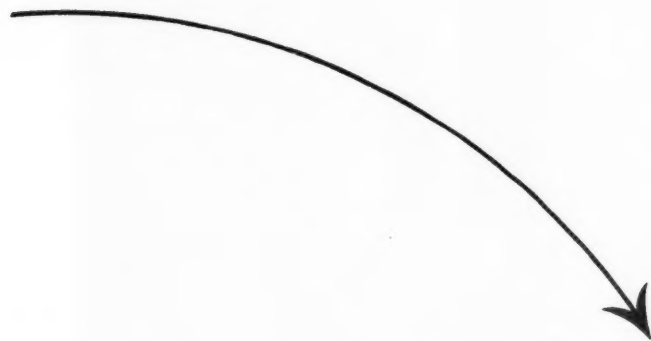
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Figs. 29A, 29B. Neurofibroma simulating an adenoma of the isthmus of the thyroid. This patient had several other subcutaneous as well as intraspinal neurofibromata.



Fig. 31 (Left). Sebaceous cyst of the neck.

Fig. 32 (Right). Sebaceous cyst. Note the punctum.

3. *Swellings of the Lateral Lobes of the Thyroid.* These usually present as anterior triangle swellings and will be dealt with later.

Diffuse enlargements of the thyroid occupy the midline as well as the anterior triangles and, if symmetrical, may justifiably be classed

as median swellings of the neck (Fig. 33). These thyroid swellings, however, are more conveniently dealt with under the heading of *Swellings of the Anterior Triangle.*

Occasionally an adenoma of a lateral lobe may enlarge medially and appear as a para-



Fig. 33 (Left). Diffuse enlargement of the thyroid.

Fig. 34 (Right). Adenoma of the right lobe of the thyroid encroaching on the midline and displacing the trachea to the left.

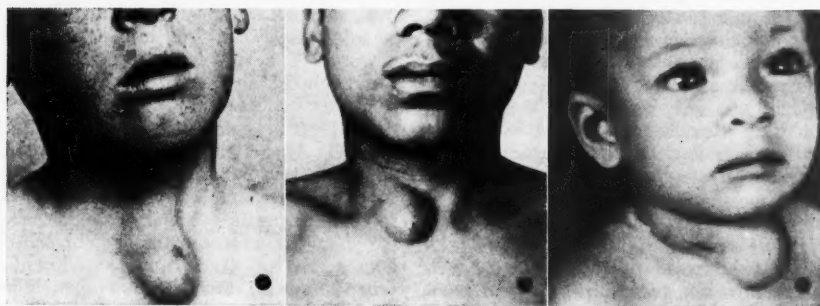


Fig. 35 (Left). Large submental cystic hygroma.

Fig. 36 (Right). Infected submental cystic hygroma.



Fig. 37. Submental cystic hygroma with extension into the floor of the mouth. The buccal component is sometimes referred to as a ranula (see text).



Figs. 38 (Left), 39 (Middle), 40 (Right). Unusual types of "branchial cyst" extending well down the neck and presenting as apparently midline swellings.

median or midline swelling (Fig. 34). Careful palpation will reveal marked lateral displacement of the trachea in such cases, which serves to differentiate them from similar tumours of the isthmus or pyramidal lobe.

4. Congenital Malformations: (a) *Cystic Hygromas.* These malformations are fairly common in infants and children. They occur in all parts of the neck and will be dealt with in greater detail in a later section. Occasionally a cystic hygroma occupies the midline of the neck, the usual situations being the submental triangle and the suprasternal fossa.

Submental hygromas (Figs. 35 and 36) are

more frequently paramedian than truly midline. They usually extend into the floor of the mouth and therefore produce not only a swelling in the neck but also a swelling under the tongue (Fig. 37). The buccal component (which is usually small, bluish in colour and, like the subcutaneous portion, brilliantly translucent) is often referred to as a 'compound' or 'plunging' ranula. We feel that such terms are misleading and only cause confusion by over-emphasizing the importance of the buccal swelling, whereas the neck swelling usually forms by far the larger part. In our experience the true ranula, which is lined by epithelium and arises in the glands of the floor

of the mouth, is an entirely different entity. The latter is less frequent, usually occupies one side of the floor of the mouth, never extends into the neck and is easily cured by a minor surgical procedure. The hygroma, on the other hand, is not only much more common but presents a formidable task as far as surgical excision is concerned.

(b) '*Branchial Cyst*.' Although branchial cysts usually present as clearly defined lateral swellings of the neck (and will be described later), we have had examples of large cysts which have extended well down towards the

root of the neck and gave the appearance of a midline swelling on casual inspection (Figs. 38, 39 and 40). Palpation of the swellings, however, revealed that they extended upwards and laterally to disappear under cover of the sternomastoid.

OPSOMMING

Swelsels in die vel en die subkutane weefsels wat klinies na middellyn-swelsels van die nek lyk, word geïllustreer en beskryf.

Aandag word ook bestee aan swelsels van die laterale kwabbe van die skildklier en aangebore misvormings.

HIPOGLIKEMIE EN DIE HIPOGLIKEMIESE SINDROOM

BESPREKING VAN TWEE GEVALLE

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Hipoglikemie, hiperinsulisme en hipoglikemiese sindroom is terme wat dikwels as sinonieme gebruik word. Indien dit korrek is, behoort hipoglikemie altyd die gevolg te wees van 'n verhoogde insulienproduksie, wat ons egter weet nie die geval is nie.

Wilder¹ was die eerste om 'n eilandselgewas met aanvalle van hipoglikemie, te beskryf. Sederdien het baie sulke pasiënte suksesvolle snykundige behandeling ondergaan.

Dit het egter gou duidelik geword dat die meeste persone met 'n hipoglikemiese beeld, geen eilandselgewas of ander bewyse van hiperinsulisme het nie, en so het 'n groot nuwe groep, die sogenaamde funksionele hipoglikemieë, ontstaan, sonder duidelike simptomatologie, spesifieke orgaanpatologie of definitiewe terapie.

Die hipoglikemiese sindroom is blykbaar die gevolg van veranderinge in die breinmetabolisme² en hipoglikemie is dus eintlik meer 'n funksionele toestand as 'n patologiese entiteit. Enige toestand wat dus die bloedsuiker-konsentrasie voldoende onderdruk mag 'n hipoglikemiese beeld laat ontwikkel, soos b.v. die verstoring van die funksie van die lewer, van verskeie endokriene klieren of van dit outonome senuweesistiem. Die lewer beklee eintlik 'n sleutel posisie sover dit die homeostase van die bloedsuiker-konsentrasie aangaan.

Die kliniese beeld van die hipoglikemiese sindroom verskil baie van persoon tot persoon. Soms is die enigste klage die van swakheid,

bewerigheid en hoofpyn, terwyl by ander daar aanvalle van bewussynsverlies is.

Kauver en Goldner³ beskou bloedsuikerwaardes van 50 mg. of minder per 100 ml. bloed as 'n bewys van hipoglikemie. Simptome behoort dus te ontwikkel as die bloedsuiker tot onderkant 50 mg. per 100 ml. bloed daal. Daar is egter baie uitsonderinge op hierdie reël. Diabetiese pasiënte kla b.v. soms van simptome wat nie te onderskei is van 'egte hipoglikemiese simptome' nie, terwyl die bloedsuiker-konsentrasie normaal of bokant normaal is. Aan die anderkant mag die bloedsuiker-konsentrasie tot 20-30 mg. per 100 ml. daal (eilandselgewas) sonder dat enige simptome ontwikkel. Tussen hierdie twee uiterstes vind ons dan persone wat ly aan sogenaamde hipoglikemiese vermoënis met swakheid, tremore, hartkloppings, vrees en oortollige sweet met 'n normale bloedsuiker-konsentrasie. Die feit is dat genoemde simptome maklik opgehef kan word deur glukose per os te neem.

Verskillende verklarings vir bogenoemde skynbare teenstrydighede is gegee,³ bv. dat:

1. Die suiker-konsentrasie in die bloed nie 'n juiste weergawe is van die suiker-konsentrasie in die breinselle nie;
2. Die bloedsuiker-konsentrasie self voldoende mag wees, maar dat die meganisme wat die suiker oordra na die weefselselle (breinselle) beskadig is;
3. Dit moontlik is dat die skielike verandering in bloedsuiker-konsentrasie (van hoër na laer), eerder as die suiker-konsentrasie as sulks, verantwoordelik is vir die simptome, en so meer.

Dit is natuurlik moontlik dat ons soms net

'n gelokaliseerde glukose-gebrek in die serebrum mag hê.

Nadat 'n diagnose van 'hipoglikemiese sindroom' eenmaal gemaak is, moet besluit word of dit 'n funksionele, of 'n organiese oorsprong het; veral moet sterk pogings aangewend word om te onderskei tussen hipoglikemie as gevolg van 'n eilandselgewas en 'funksionele hipoglikemie'. Punte van spesiale differensiële diagnostiese waarde in hierdie verband, is:

(a) 'n Eilandselgewas is 'n egte neoplastiese siekte, en is gewoonlik vinnig progressief, sodat die aanvalle meer frekwent en intens word;

(b) Die afkeiding van insulien deur die gewas is onafhanklik van die metaboliese meganismes wat bloedsuikerkonsentrasie beheer en gevolglik kan aanvalle feitlik enige tyd van die dag of nag voorkom. Funksionele hipoglikemie, daarenteen, ontwikkel gewoonlik as 'n reaksie teenoor koolhidraat-inname, of as gevolg van emosionele of fisiese 'stress'.

Wilder *et al.*⁴ en Whipple⁵ het die volgende punte aanbeveel om 'organiese hipoglikemie' te onderskei van 'funksionele hipoglikemie':

1. 'n Geskiedenis van voorafgaande goeie gesondheid;

2. 'n Geskiedenis van aanvalle wat 'n definitiewe patroon volg, en aankom gedurende vasperiodes;

3. 'n Vastende bloedsuikerkonsentrasie van 50 mg. of minder per 100 ml. bloed;

4. Onmiddellike herstel na toediening van glukose;

5. Onverdraagsaamheid teenoor vas — indien nodig, moet die vas vir 48 uur aanhou.

Tor dusver is daar nog geen eenvoudige toets waarmee die insulienkonsentrasie in die bloed bepaal kan word nie.

Waardevolle gegewens wat mag help om 'n finale diagnose van funksionele hipoglikemie te maak, sluit in:

(a) 'n Geskiedenis van episodes wat 'n verwantskap toon tot voedselinname;

(b) Toleransie teenoor insulien;

(c) Toleransie teenoor glukose;

(d) Die epinefrien-toets;

(e) Die bepaling van die bloedsuikerkonsentrasie tydens 'n episode mag van waarde wees.

GEVAL I

R. P., 'n blanke man, 51 jaar oud, was gesond tot Augustus 1952, dog toe het hy 'n dowwe knagende pyn in die epigastrium ontwikkel wat uitgesprei het na die borskas en linker oksel. Die pyn het ongeveer 2½ uur na maaltye aangekom en is verlig deur antisuurmiddels. Die pasiënt het erken dat hy in finansiële moeilikheid verkeer en dat sy huwelikslewe baie ongelukkig was.

'n Definitiewe diagnose is nie met die eerste besoek gemaak nie, en die pasiënt is na 'n internis verwys, wat onder andere gesoek het vir 'n maagulkus, 'n koronêre trombose, 'n dissekerende aneurisme van die aorta, patologie

van die werwelkolon, mediastinale emfiseem, perikarditis, long-embolus, en so meer, dog al die spesiale ondersoeke was negatief.

R. P. is sonder 'n definitiewe diagnose terug na sy werk, maar sy toestand het intussen progressief erger geword en 3 maande later was sy vernaamste klagtes dat hy teen ongeveer 10.30 vm. en 3.30 nm. so moeg was dat hy geen moed gehad het om iets te doen nie. Die moegheid het gepaard gegaan met 'n gevoel van onwerklikheid en terneergedruktheid, en die pasiënt het erken dat hy selfmoord sou gepleeg het as hy net die energie gehad het. Die pasiënt is weer na die internis verwys en 'n diagnose van psigiese spanning gepaard met histerie is nou gemaak. Behandeling is voorgeskryf, dog dit het slegs tydelike verbetering gebring. Tydens 'n besoek ongeveer 2 maande later is opgemerk dat R. P. meer sweet as wat mens redelikerwys sou kon verwag, dat sy polsspoed 94 per minuut is, en dat sy temperatuur normaal is. Dit het ons op die gedagte van 'hipoglikemiese sindroom' gebring. Besluit is om 20 c.c. van 'n 5% glukose oplossing binne-aars toe te dien en nog voordat die inspuiting voltooi was, het die pasiënt half bewusteloos geword; na 30 uur van vas, was die bloedsuikerkonsentrasie normaal. 'n Glukose-toleransie toets het 'n bloedsuikerkonsentrasie van 50 mg. per 100 ml. na 2 uur getoon (Tabel 1). Met 'n opvolgende toets, is min of meer dieselfde resultate gekry.

GEVAL II

L. C., 'n manlike mediese student, 20 jaar oud, het Augustus 1954 gekom met die verhaal dat hy 14 dae vantevore siekerig begin voel het, 'n geneesheer besoek het, en dat 'n diagnose van griep gemaak is waarvoor hy elke dag 600,000 E. Crysticillin, vir 8 dae lank binnespiers ontvang het. Die toestand het 'n bietjie verbeter, maar teen ongeveer die sesde dag na die laaste inspuiting, het die pasiënt 'n dowwe aanhoudende pyn in die epigastrium ontwikkel, wat na die borskas versprei het, veral na die prekordiale gebied. Hierdie aanvalle het gewoonlik so teen 9.30 vm., 3 nm. en 8 nm. aangekom, vir 'n uur of twee aangehou, en dan geleidelik bedaar. Die aanvalle het gepaard gegaan met hartkloppings, benoudheid en 'n gevoel van dreigende gevaar, en was gewoonlik in die aand die ergste. By twee geleenthede (albei in die aand) was die pasiënt oortuig dat hy sou sterf en het sy ouers 200 myl ver laat hom om van hulle afskeid te neem.

Gedurende so 'n episode was die temperatuur van die pasiënt gemiddeld 99.5° F., die

polsspoed 96 per minuut, en die hande was klammer as wat mens sou verwag.

Volgens L. C. se vader het sy seun 5 jaar vantevore malaria gehad, wat volkome herstel het na behandeling; volgens hom het die huidige aanvalle baie ooreengestem met die van 5 jaar gelede. Daar is toe spesiaal gesoek vir malaria parasiete, malta-koors, maagkoors, urienafwykinge en lewerletsels, maar al hierdie toetse, sowel as fotos van die longe en maag en 'n elektrokardiogram was negatief.

Na aanleiding van die ondervinding met R. P. is die bloedsuikerkonsentrasie toe bepaal tydens so 'n aanval, en 'n waarde van 45 mg. per 100 ml. is gekry. Na 40 uur se vas, was die bloedsuiker 84 mg. per 100 ml. Die toediening van glukose binne-aars het 'n dramatiese reaksie uitgelok. (Vir die glukose-toleransie sien Tabel 1).

TABEL 1: GLUKOSE-TOLERANSIE VAN R. P. EN L. C.

Monster Bloed	Mg. Bloedsuiker per 100 ml. Bloed (R. P.)	Mg. Bloedsuiker per 100 ml. Bloed (L. C.)
Vastend	74	82
$\frac{1}{2}$ uur	107	112
1 uur	87	80
2 uur	50	45

By beide die voorgaande gevalle is 'n diagnose van funksionele hipoglikemie gemaak. Die onmiddellike oorsaak vir die aanvalle was 'n relatiewe oormaat insulien, maar wat die aanleidende oorsaak was, is nie heeltemal duidelik nie. Volgens die kliniese en spesiale ondersoeke het die lewer, skildklier en bynierskors van beide pasiënte normaal funksioneer.

Dit is moontlik dat psigiese 'stress' 'n rol gespeel het, te wete die finansiële en huislike

probleme by R. P. en die naderende eksamens by L. C., maar algemeen word aangeneem dat 'stress' die afskeiding van sowel adrenalin as bynierskors-hormone in die hand werk. Ons sou dus eerder 'n verhoogde bloedsuikerkonsentrasie verwag het.

Oor die algemeen beskou, wil dit voorkom asof die eilandsisteem 'n verhoogde gevoeligheid ontwikkel het teenoor 'n skielike styging in bloedsuikerkonsentrasie, maar presies waarom is nie duidelik nie—of moet ons die fout by die insulien-antagoniste gaan soek, soos b.v. 'n tekort aan hiperglikemiese glikogenolitiese faktor?

BEHANDELING

Geen spesifieke behandeling is toegepas nie, behalwe dat beide pasiënte op 'n dieet geplaas is soos deur Conn⁶ aanbeveel word. Met hierdie behandeling het hulle tot dusver baie goed gevaar.

OPSOMMING

Die hipoglikemiese sindroom is kortliks bespreek, en 2 gevalle van funksionele hipoglikemie is beskryf.

SUMMARY

The hypoglycaemic syndrome is discussed briefly and 2 cases of functional hypoglycaemia are described.

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THE INFLUENCE OF CORTISONE ON GANGLION CELLS

A PRELIMINARY REPORT

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If ganglion cells show chromophobia as a result of axon reaction, prolonged electrical stimulation, fatigue or stimulant action of drugs such as strychnine, restoration to normal will set in as soon as the disturbing factor has been eliminated. This re-synthesis of basophilic material (Nissl substance) may proceed until

a state of slight chromophilia has been reached. The cell then returns to the state of normal basophilia. The chromophilia observed after the action of certain depressant drugs is never seen in animals which have not been subjected to such actions.

These facts prompt the question of what

factors are involved in the control of the synthesis of cytoplasmic ribonucleoprotein of ganglion cells. It can be anticipated that, as in many other physiological processes, a balance is reached by the interaction of a number of factors, some of which can be called positive in action, and others negative, to indicate the respective increase and decrease in cytoplasmic basophilia. Such a regulating mechanism, if it exists, is probably endocrine and nutritional. Certain vitamin deficiencies are accompanied by a severe loss of Nissl substance, indicating that the corresponding vitamins probably promote the synthesis of ribonucleoprotein. Hormones which exert the opposite effect in ganglion cells are not at present known to exist.

EXPERIMENTAL DATA

Young rats were subjected to fairly high doses of cortisone.*

Two groups of rats, 4 weeks old were used. Each group contained 10 males and females each. One group served as a control and the animals of the other group received 5 mg. cortisone subcutaneously every second day. After 3 weeks, 3 animals were sacrificed from each group. This was repeated every second week thereafter. Only the results in the first 6 animals of each group are reported.

The animals were killed by chloroform, perfused with 5% acacia gum-saline and the tissues fixed by perfusion with formalin, dihydrostreptomycin acetic acid in 5% acacia gum-saline. Paraffin sections at 7 microns were stained either with Ehrlich's haematoxylin-eosin or brilliant cresyl blue.

RESULTS

The following observations were made:

1. *Cellular Membrane.* This structure is less distinct than in the cells of the control animals.

2. *Nissl Bodies.* All cells without any exception showed a severe loss of basophilic granules. This was particularly evident in the anterior column motor neurons with their central 'chromatolysis'. In the animals under cortisone treatment this loss is incomplete in the motor neurons, but several of the comisural cells of the lateral column were found to be completely devoid of basophilic cytoplasmic material. In the animals under treatment for 5 weeks this sign was even more pronounced.

* The initial results are reported now. A more complete description of the observations of the whole series will appear later.

3. *Nucleus.* The stainability of the nuclear basophilic material does not seem to be affected. The position of the nucleus in the perikaryon is eccentric in many cells, sometimes making contact with the cellular membrane. This sign is more pronounced in the lateral column cells than in the motor neurons.

4. *Nuclear Membrane.* In all cells the nuclear membrane is well defined. In many cells a so-called nuclear cap is observed, although this nuclear cap sometimes shows a poor stainability, suggesting a relative poverty of nucleotides.

5. *Nucleolus.* In many cells its position has changed to an extreme eccentric position of direct contact with the nuclear membrane. Again this is particularly found in the lateral column cells. No measurements have yet been made of the nucleoli, which show a vacuolated appearance.

6. *Paranucleolar Bodies.* No difference was found between the male and the female animals of the cortisone-treated group. In a large number of cells double or triple paranucleolar bodies have been observed, some of them reaching a diameter of nearly half that of the nucleolus itself. Their positions varied from direct contact with the nucleolus to extreme eccentricity. In general there was an increase in the basophilic material of the nucleoplasm. The nuclear pattern suggested a larger number of chromocentre areas for ribonucleoprotein synthesis as compared with the normal pattern.

DISCUSSION

The changes described in the ganglion cells strongly suggest that cortisone decreases the cytoplasmic ribonucleoprotein content of ganglion cells. At the same time there is an increased activity in the centres for ribonucleoprotein synthesis. It cannot yet be decided whether the increased synthesis is a direct result of the depletion of the basophilic material, which is most likely, or whether this increased activity is due to a stimulant action of the drug itself, which is unlikely.

It is concluded that cortisone may play a role in the mechanism governing the cytoplasmic ribonucleoprotein content of the ganglion cells. Several sets of experiments to study the effects of other hormones are in progress. The results will be reported later.

SUMMARY

1. The ganglion cells of young rats (injected with fairly large doses of cortisone) develop loss of cytoplasmic basophilia.

2. Changes in the position of the nucleolus and the position, number and size of the para-

nucleolar bodies indicate an increased synthesis of ribonucleoprotein.

3. It is concluded that cortisone may play a role in the mechanism regulating the content of cytoplasmic ribonucleoprotein of ganglion cells

This has to be confirmed by a greater number of observations.

This study has been made possible by a research grant from the Council for Scientific and Industrial Research, Pretoria.

OPSOMMING

1. By jong rotte ontstaan daar 'n verlies van sitoplasmiese basofiele senuknoopselle onder invloed van kortisoan in betreklik groot dosisse.

2. Veranderings in die nukleêre patroon vir sover dit die posisie van die kernliggaampies en die posisie, aantal en grootte van die paranukeêre liggame betref, dui op 'n verhoogde sintese van ribonukleoproteïene.

3. Daar word tot die gevolgtrekking geraak dat kortisoan bes moontlik 'n rol speel in die meganisme wat die sitoplasmiese ribonukleoproteïen-inhoud van die senuknoopselle reguleer. Hierdie feit sal gestaaf moet word deur 'n groter aantal waarnemings.

PREPARATE EN TOESTELLE

BOCASAN

'N DOELTREFFENDER BEHANDELING VIR MOND-INFEKSIES

Bocasan is 'n unieke preparaat wat sowel sy samestelling as sy voorbereiding betref, en kan vir 'n groter verskeidenheid van aandoenings gebruik word as enige ander dergelike preparaat. Dit is feitlik waterstofperoksied in poeivorm. Dit is antisepties en kiemdodend. Dit versleg nie gou nie en word

beskikbaar gestel vir gebruik in 'n stabiele, gekonsentreerde poeivorm. *Bocasan* bevat slegs 2 bestanddele—natriumperboraat en natriumbitartraat—verenig in 'n enkele stabiele samestelling wat (as water bygevoeg word, of as dit in aanraking met enige organiese stof kom) veel meer suurstof vrystel as die gewone perboraatmengsels.

Bocasan - samestelling bevat, gewig vir gewig, 30% beskikbare suurstof, of 3 keer soveel soos waterstofperoksied U.S.P.

Die voordele van so 'n konsentrasie van nascente suurstof in 'n stabiele poeier lê voor die hand as die effek van suurstof op ontlaadingsweefselprosesse in gedagte gehou word.

Bocasan-samestelling het so te sê geen brandende of prikkelende effek op die slymvliese nie.

Die konsentrasie en stabiliteit van *Bocasan*-samestelling maak dit 'n middel wat vir 'n groot verskeidenheid van doeleindes gebruik kan word, en die feit dat dit nie maklik sleg word nie, word geëwenaar slegs deur die gemak waarmee die poeier tot enige verlangde sterkte verdun kan word.

Die suksesvolle aanwending daarvan vir die bestryding van etlike onlangse uitbrekings van loopgraafmond getuig ook van die feit dat hierdie produk op 'n steeds groter skaal deur tandartse en geneesherse gebruik word.



Die gebruik daarvan vir die behandeling van piorree, loopgraafmond, tandvleisontsteking en ander ontlaadingsmondprosesse lê voor die hand. Dit kan aangewend word deur die oplossing regstreeks in die tandvleis en rondom die tandholte in te spuit. Die voordele verbonde aan die aanpassing van die sterkte van die oplossing by die behoeftes van die pasiënt word baie duidelik deur die pas genoemde gevalle toegelig.

Dit is ook nuttig as 'n aanvullende behandeling wat die pasiënt wat aan sulke toestande ly, by sy eie huis kan toepas. Die feit dat dit die tande witter maak is 'n addisionele voordeel, en hierdie metode om nascente suurstof te ontwikkel deur die gebruik van die tartraat het 'n stadige maar nietemin gewisse losmakende effek op die opgehoopde tandsteenlae op die tand self. Dit is veral van groot belang by die behandeling van piorree, loopgraafmond en tandvleisontsteking waar die ophoping van tandsteenlae op die tande die doeltreffendheid van enige vorm van behandeling teëwerk.

Verspreiders: Muller & Phipps South Africa (Pty.) Ltd., Posbus 2207, Johannesburg.

RITALIN (CIBA)

'N PSIGO-ANALEPTICA

Ritalin (feniel-(α -piperidiel)-metielasetaat-hidrochloried) besit eienskappe wat dit êrens tussen die psigomotoriese amiene en kaffeïen plaas.

Farmakologie: Eksperimenteel stimuleer *Ritalin* die psige en verhoog beweeglikheid sonder verlies van koördinasie. Dit het 'n opwekkende effek as dit toegedien word ná sekere verdowingsmiddels, en dit stimuleer ook die asemhaling, veral wanneer die reaksie van die asemhalingsentrum verlaag is deur sentrale inhibisiedmiddels, bv. morfiën.

Ritalin het 'n geringe pressoreffek, maar dit gaan nie vergesel van enige opvallende perifere simpatomimetiese aksie nie (R. Meier, F. Gross en J. Tripod: Klin. Wschr., 32, 445, 1954).

Kliniese studies: Die kliniese resultate (A. Drassdo, en M. Schmidt: Med. Klin., 49, 892, 1954; Med. Mschr., 8, 306, 393, 1954) van die proefnemings in verband met opwekkende effek en verbeterde prestasies is veral indrukwekkend. Op die toediening van twee tablette van 10 mg. volg daar 'n stimulerende effek wat van 4-6 uur lank duur.

Die verbetering van geestesvermoë is duidelik aan die lig gebring tydens sorgvuldig gekontroleerde berekeningstoetse wat met en sonder *Ritalin* gedoen is. Verbeterings in prestasie het gewissel van 10.5%—92% na die gebruik van *Ritalin*. In 'n uiterste geval was die verbetering 330%.

Die Perifere Effek van Ritalin: Van die 60 persone wat getoets is, is 'n geringe toename in die asemhalingsfrekwensie na die toediening van 10 mg. *Ritalin* by slegs 5 opgemerk. By die ander 55 het die asemhaling normaal gebly. Die polsnelheid van 24 het toegeneem; by 11 het dit afgeneem, en by 25 het dit normaal gebly.

In teenstelling met die bevindings tydens die eksperimente met diere het 28 van die 60 persone op *Ritalin* gereageer met 'n geringe daling van bloeddruk, maar die pols het vol gebly. Agtien pasiënte het op *Ritalin* gereageer met 'n verhoging van sistoliese druk, en by 'n aantal het die verskil tussen sistoliese en diastoliese druk gelyktydig toegeneem.

Prestasie en Stemming: *Ritalin* is in sy wese 'n sentrale stimuleermiddel. Dit verbeter sowel die

stemming as die prestasies. Die pasiënt word meer selfversekerd. Die toename in inisiatief en die gedagtevloed verbeter, en die vermoë om te konsenteer bly terselfdertyd onaangetas. Simptome van uitputting verdwyn.

Toepassing: *Ritalin* is bedoel vir die behandeling van pasiënte wat aan toenemende uitputting, neerslagtigheid of geestemoegheid ly. *Ritalin* is besonder waardevol by die behandeling van versteurings van 'n oorwegend emosionele aard, en is ook 'n psigoanaleptica tydens herstel.

Dosis: Die stimulerende effek word gewoonlik duidelik waargeneem nadat die pasiënt een tablet van 10 mg. geneem het; 'n enkele dosis van 20 mg. kan soms nodig wees. Met sulke klein dosisse is daar geen bykomstige effekte nie. As *Ritalin* na 4-uur nm. geneem word, kan dit slaaploosheid tot gevolg hê. *Ritalin* behoort nie ononderbroke oor lang tydperke geneem te word nie.

Verpakking: Tablette van 10 mg. Bottels van 30 en 150.

Agente vir Ciba Limited: Sana Limited, Posbus 3951, Johannesburg.

PREPARATIONS AND APPLIANCES

BOCASAN

A MORE EFFECTIVE TREATMENT FOR BUCCAL INFECTIONS

Bocasan is a preparation unique in composition and processing, and capable of a wider range of application than any other similar preparation. It is virtually hydrogen peroxide in powder form, is antiseptic, germicidal, does not readily deteriorate and is available for use in a stable, concentrated powder form.



Bocasan contains only 2 ingredients, Sodium Perborate and Sodium Bitartrate, combined into one stable compound, which (on the addition of water and/or contact with any organic material) releases oxygen in a quantity much in excess of ordinary perborate mixtures.

Bocasan compound contains weight for weight 30% available oxygen or 3 times as much as Hydrogen Peroxide U.S.P.

The advantages of such a concentration of nascent oxygen in a stable powder are very apparent for the effect of oxygen on degenerative

tissue processes.

Bocasan compound is relatively free from burning and irritation to membranes.

The concentration and stability of *Bocasan* compound lend greater scope to its usefulness, and the fact that it does not readily deteriorate is only equalled by the ease with which the powder may be diluted to any required strength.

Its successful application in helping to bring under control several recent outbreaks of trench mouth also attests to the growing utilization of this product by the dental and medical professions.

Its application in the treatment of pyorrhoea, trench mouth, gingivitis and other degenerative buccal processes is self-evident. It may be used by direct injection of the solution under the gums and around the tooth socket, when the advantage of being able to adjust the strength of the solution becomes increasingly evident.

It is also a useful supporting treatment for the patient to employ at home in these conditions. Its action in whitening teeth is an advantage, and this method of evolving nascent oxygen by the use of a tartrate has a slow but nevertheless sure effect of loosening accumulated tartar deposits on the tooth itself. This is particularly an advantage when treating pyorrhoea, trench mouth and gingivitis where the accumulation of tartar deposits on the teeth retard the effectiveness of any form of treatment.

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RITALIN (CIBA)

A PSYCHO-ANALEPTIC

Ritalin (phenyl-(α -piperidyl)-methylacetate hydrochloride) has properties which place it somewhere between the psychomotor amines and caffeine.

Pharmacology: Experimentally *Ritalin* stimulates the psyche and improves motility without loss of co-ordination. It has a rousing effect when applied after certain narcotics, and also stimulates the respiration, in particular when the response of the respiratory centre is lowered by central inhibitors, e.g. morphine.

Ritalin has a mild pressor effect, but this is not accompanied by any marked peripheral sympathomimetic actions (R. Meier, F. Gross and J. Tripod: Klin. Wschr., 32, 445, 1954).

Clinical Studies: Clinical results (A. Drassdo and M. Schmidt: *Med. Klin.*, **49**, 892, 1954; *Med. Mschr.*, **8**, 306, 393, 1954) on the rousing effect and improved performance are particularly impressive. One or two tablets of 10 mg. produce stimulation lasting 4-6 hours.

The increase in mental performance is very clearly revealed in carefully controlled calculation tests solved with and without *Ritalin*. Improvement in performance ranging from 10.5%—92% was demonstrated after *Ritalin*. In an extreme case the improvement reached 330%.

Peripheral Effect of Ritalin: Of 60 test subjects only 5 showed an increase of the respiratory frequency—mild in character—after 10 mg. of *Ritalin*; respiration remained normal in the other 55. The pulse was accelerated in 24, slowed down in 11, and remained normal in 25.

In contrast to the findings obtained in animal experiments, 28 of the 60 subjects responded to *Ritalin* with a slight drop of pressure, the pulse remaining full, 18 patients responded to *Ritalin* with an increase of systolic pressure, and in a number of these the difference between systolic and diastolic simultaneously increased.

Performance and Mood: *Ritalin* is basically a central stimulant. It enhances the mood and improves the performance. The patients become more self-assured. They gain in initiative, and the flow of thought improves while at the same time the ability to concentrate remains unimpaired. Symptoms of fatigue vanish.

Application: *Ritalin* is intended for the treatment of patients suffering from increased fatigability, depression and mental exhaustion. *Ritalin* is very valuable in disturbances of predominantly emotional character, and also as a psycho-analeptic in convalescence.

Dosage: The stimulant effect is usually clearly observed after taking one tablet of 10 mg.; a single dose of 20 mg. may occasionally be required. Side effects are not encountered with these small doses. Insomnia may result if *Ritalin* is taken after 4 p.m. *Ritalin* should not be taken continuously for long periods of time.

Packages: Tablets of 10 mg. Bottles of 30 and 150.

Agents for Ciba Limited: Sana Limited, P.O. Box 3951, Johannesburg.

THE OOSTHUIZEN PLAN FOR THE EXTENSION OF RADIOTHERAPEUTIC SERVICES IN THE TRANSVAAL

Centralization of radiotherapy is mainly dictated by financial considerations, because it is very uneconomic to install and man expensive equipment in rural areas without a sufficiently large turnover of clinical material. But there is no need to adhere to this principle so rigidly as to deprive non-urban communities of adequate facilities for the early, efficient and inexpensive detection and treatment of some of the more accessible cancers (e.g. tongue, lip, cheek and even carcinoma of the bladder, when suitable conditions exist for intra-cavitary treatment). Many cancers do indeed fall into such an accessible category.

This enlightened view in fact found expression in Dr. Maurice Weinbren's *Memorandum to the Gluckman Health Services Commission* as far back as 1943. Dr. Weinbren stated, *inter alia*: 'One . . . has to strike a balance between the needs and convenience of the public and the expense and efficiency of radiotherapeutic centres.'

Through the far-sighted efforts of Prof. S. F. Oosthuizen, the Transvaal Provincial Administration has recognized and applied the truism that Mahomet must go to the mountain. Experienced radiotherapists from the 2 large centres in the province have been appointed to pay regular weekly or fortnightly visits to outlying centres. The visiting therapist

can advise local practitioners on the screening of cases suitable for treatment on the spot or more suitable for transfer to the nearest city. Moreover, a therapist who can needle a tongue in Johannesburg or Pretoria can do so just as easily in Klerksdorp or Barberton, and the general practitioner can, if necessary, remove the needles later.

With the introduction of radio-isotopes and the greater availability of radon and radium, a considerable therapeutic programme is now possible (as the Transvaal has appreciated) away from the population concentrations in Johannesburg and Pretoria. There is the important advantage also that the patient's domestic and business life is not disrupted, his emotional stress is lessened and the expense (both for him and the State) is markedly diminished.

This progressive pilot scheme has been initiated in Klerksdorp, Potchefstroom, Vereeniging, Standerton, Barberton, Witbank, Ermelo and Pietersburg.

It is a forward-looking provision particularly appropriate for the communities scattered thinly over vast areas of our country. The Oosthuizen plan for the Transvaal already embraces a diagnostic service for outlying areas and is now likely to be a blue-print of the shape of things to come for the rest of the country.

OVERSEAS SUPPLIES OF ANTI-POLIO VACCINE FOR SOUTH AFRICA?

The U.S.A. Government lifted the control system on the distribution of anti-polio vaccine on 1 August 1956. It therefore seems probable that substantial quantities of a rigorously tested vaccine (safe and of proven

efficacy) may become available in South Africa within the next few weeks. Latest figures indicate that American manufacturers have already (between them) produced and distributed over 81 million c.c. of the vaccine.

CORRESPONDENCE

A NEW APPROACH TO CHEST PAIN IN GENERAL AND CORONARY THROMBOSIS IN PARTICULAR

To the Editor: It is with some diffidence that I present these suggestions. Perhaps I ought to label

them *Random Thoughts*, for that is what they really are. They represent big ideas built around a small number of cases; small only because a G.P. sees a cross-section of the people's illnesses and no more than its correct proportion of any particular one,

even though he is particularly interested in it. Nor have I any scientific data to offer, such as seem to give weight to every article on any subject that appears in any medical journal, and without which no article seems complete. I have not even kept records. All I have to submit are the memory of a few cases, and theories which have nothing more to back them than mere results and reason.

But when the reader puts this down he may say to himself: 'Well, well! There might be something in what this fellow says. Why did he keep it to himself all these years? If what he says is right, look how many lives could have been saved. That's unethical behaviour.' As a matter of fact I did approach one of our foremost cardiologists 10 years ago and asked him to investigate my speculations; for he had a hospital practice of heart cases only, an ideal ground for this purpose. But he was politely uninterested.

However, last week, browsing through back numbers of this Journal I came across two quotations in an *Annotation** which made me think I was probably on the right track after all, and that I should make them public for what they were worth.

Twenty years ago (in 1936) a patient called me urgently for a pain in the chest. The pain had started mildly but had worsened so rapidly that by the time I reached him he lay groaning in agony. Two things struck me when I examined him: he was not shocked and the pain did not radiate down the left arm. I had treated him for an angioneurotic swelling of the tongue some months before and it flashed across my mind that this might be an angioneurotic swelling of a thoracic viscus. I gave him 10 minims of adrenaline hypodermically. If it failed to have any effect within a few minutes, I could always fall back on morphine. To my amazement the pain began to subside far sooner than it would have done with morphine and within 10 minutes he had recovered completely.

That was the first but not the only attack he had. After that he carried a syringe and adrenaline wherever he went and during the next 10 years had many occasions to use them. Each time the pain disappeared, as though by magic, and he soon learned that the earlier he took the injection the better.

(The name 'angioneurotic oedema' is cumbersome and as it will be used many times in the following paragraphs I propose to shorten it to 'anoedema', which seems amply descriptive and better than the old name 'Quincke's oedema').

Anoedema as a cause of chest pain has never been admitted. Why not? Surely that is what one would expect from a condition which can cause localized swellings in any tissue of the body—perhaps even the brain. Its occurrence in the deeper structures cannot be excessively rare, for I have seen one probable and 2 unequivocal cases involving a chest viscus, since I have been on the lookout

for it, besides several in other deep structures, the nature of every one of which was proved by its response to adrenaline. One of the latter was in a man who complained of 'indigestion' that felt 'like a lump' which obstructed the food he swallowed when it reached his stomach. It did not affect his appetite or health in the least. It stayed for several days, sometimes weeks, then would disappear for months. It was never painful, probably because the tissues of the oesophagus are easily stretched, and he might not have known it was there but for the discomfort in swallowing. It always disappeared within a few minutes of an injection of adrenaline. In another case the patient (a female) used to have recurring, acute right-sided pelvic pain, but never a rise in temperature or pulse rate, or any other sign or symptom which might indicate its cause. Here I was led to the diagnosis by a history of swellings in the cheek years before, which stopped just about when the pelvic pain began. I concluded that she suffered from a swelling inside the capsule of the ovary and, as judged by the response to adrenaline, that seemed the right answer.

One associates anoedema with the eyes, the tongue, the cheeks and the scrotum, because there it is visible and one has no doubt about its nature.

Some of the peculiarities of anoedema should be noted. It tends to recur in the same spot again and again for long periods, perhaps for life. When it does change, it usually favours its new site for long periods, only to move, if it does move, back to the original spot. There are exceptions—there must be—but it is the rule that anoedema is conservative in its movements. There is another rule that it seldom breaks: it attacks deeper structures as its victims grow older. One seldom sees the superficial forms in older subjects and I have never diagnosed the deeper form in anyone under 30 years.

It is said that anoedema is an analogue of urticaria and due to the same causes. In fact, it is sometimes referred to as 'giant urticaria'. That is indeed fortunate, for by studying the common, we can explain some of the vagaries of the rare.

It is known that an allergic subject might eat a food to which he is sensitive for long periods without having any reaction from it; also that persons who have never during their lifetime shown any signs of allergy, may have an attack of urticaria from a food they have eaten regularly all their lives. These reactions, or lack of reactions, are explained by assuming that the threshold of sensitivity can vary with circumstances. Again, to explain a single attack in a whole lifetime, it is assumed that there are persons who would be allergic to certain substances but have never come into contact with them; but if they did one day happen to meet (or eat) the allergen, they would experience the first allergic reaction of their lives and, if they never met (or ate) that substance again, the last.

How can pain in the chest due to anoedema be recognized? First and most obviously, anyone who gives a history of frank anoedema and presents himself with an acute pain in the chest is suspect. It is therefore important in the history to remember to ask the patient specific questions about previous swellings in the cheeks, tongue, etc. If these questions are not specifically asked we should never learn about them, because the patient is unlikely to mention them on his own. But in one who has never had obvious anoedema

* '... better results have been claimed with *l*-noradrenalin, though the mortality is still considerable.'

'Duguid believes that thrombosis is the fundamental cause of coronary artery narrowing and it is the clot, later incorporated into the vessel wall, which is the cause of the "atheromatous patch".'

[*Annotation* (1956): *Med. Proc.*, 2, 84].

before, we have to judge by the type of pain and its mode of onset. In the 2 definite cases I saw, I considered the swelling to be in the wall of the descending thoracic aorta. The pain radiated from behind the lower end of the sternum. It started with a mild, warning pricking, such as occurs in the tongue when it is about to swell. The first actual pain is like the flick of a rapier through the chest. Then there is quiet, except for the throbbing of an anxious heart. It may be several seconds before the next thrust, and from then on it comes at shorter and shorter intervals, the blade getting hotter and hotter and changing its direction each time, now to the right, now to the left, backwards, upwards, downwards, more and more rapidly until the thrusts merge into one continuous excruciating agony. At that point, say 10 minutes after the start, the upper limit of perception of pain seems to be reached, for it becomes no worse although the swelling must still be growing. It is possible that if one were to X-ray the patient's chest at that stage one would see a bulge on the wall of the aorta which, if only it threw a deeper shadow, might be thought to be an aneurysm.

This description refers to a swelling in a highly sensitive, inelastic viscus. But there are viscera within the chest, especially the lungs, which are not only insensitive to pain but are so stretchable that a swelling within them might pass unnoticed. The inner chest wall with its sensitive pleura holds a position between the two extremes and the one probable case that I saw seemed to be in that part. I only saw him in one attack, for which he consulted me on board a ship of which I was surgeon. He was on his way to see a London physician about the recurrent pain which had never been diagnosed. It had been coming at irregular intervals for some years and was located deep to the right breast. Though he had come to me for an analgesic, his certainly was not nearly as painful a case as my previous 2 cases. The robust health of the man, which certainly ruled out any serious condition of the lung or pleura, the irregular periodicity of the pain, and the fact that the amount of pain built up over a period, reminded me of an oedema. He had no history of frank an oedema, but on the strength of probability I thought it worth trying adrenaline, so I gave him an injection. He returned later to tell me the pain had gone. I was unable to follow up the subsequent history of this case.

An oedema can manifest itself for the first time in a viscus and recur there, never to move to a part of the body where it can be seen by the eye and felt by the hand, and so be recognized without hesitation. I am very certain that it does often originate in a viscus and that it is not diagnosed simply because it never occurs to the physician to consider it.

To summarize: It is possible to develop allergic reactions at any time of life for the first time. It is possible to have one attack only, or a limited number of attacks during a lifetime. There is a tendency for an oedema to strike in the same place again and again. There is a tendency for an oedema to attack deeper structures with advancing age. An oedema can occur in a chest viscus.

All these peculiarities of an oedema are important, but they are not crucial. The crucial question is: Can an oedema occur in the wall of the thoracic aorta in particular? To my way of thinking it happens without a doubt; but without absolute

proof, such as would be given by an X-ray showing a swelling on the aorta here to-day and gone to-morrow (to distinguish it from a dissecting aneurysm), one can only surmise how an oedema could cause a coronary thrombosis. Once we have the proof (and many a radiologist may have that proof in his files) we can say with some certainty that every *painful* coronary thrombosis begins with an an oedemic swelling at the root of the aorta, which would make the prognosis of that condition very much more favourable if the patient were seen early enough.

Coronary thrombosis has 2 distinct types of onset, the one heralded with excruciating pain and the other almost, if not totally, painless throughout its course. In the latter the first sign is shock; in the former shock does not develop until minutes, hours or even days after its onset; and even after shock develops, pain remains.

Coronary thrombosis is an arterial, not a venous, clotting. If it were venous one could expect oedema of the heart tissues and consequent stretching of its serous coverings, which would cause pain; but with an arterial clotting the very reverse is the case and the tissues of the infarct not only do not swell, but actually shrink. As only the serous coverings of the heart are subject to painful stimuli, one of which is stretching, there is no reason why a coronary thrombosis should cause pain at the start; later, perhaps, but not at the start. Later a pericarditis might develop over the infarct; but even then it could not be confused with the violent pain that heralds the painful type of thrombosis.

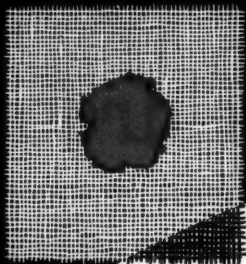
Slowing of the circulation favours thrombosis and the blood in atheromatous vessels with a narrowed lumen and rough lining, is particularly liable to clot. When that happens it gives rise to a painless thrombosis. Similarly when an embolism blocks the coronary artery there is no reason for the resultant thrombosis to be painful. The heart muscle is insensitive and even anoxic cramp cannot cause pain unless the serous covering is stretched. If this did happen, it would be of short duration.

Thus we have every reason to believe that coronary thrombosis due to atheroma or embolism is painless, and that there must be other agencies which are in themselves painful, which can cause a slowing or stasis and so a clotting of the coronary blood. The most likely of these would be an oedemic swelling of the root of the aorta, or even of the heart substance itself.

Unfortunately I have never had an opportunity of trying out my theory. If I had, I would have had results to show, confirmatory or otherwise, and would most probably have published them long before this. In all my many years of practice I have not attended a patient with a coronary episode—at least not one that I recognized. However, if I were called to one now I should not do more than ask a few questions: Have you ever had swellings of the tongue, cheek, eyes? Did the pain start mildly and build up? Does the pain feel like burning rods shooting through your chest? And if the answer were positive to any 2 of them I would inject 10 minims of adrenaline and wait expectantly while I stood ready with another syringe charged with half-a-grain of morphine.

H. J. Leviser, M.R.C.S. (Eng.), L.R.C.P. (Lond.).

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1. Owings, C. B.: The Control of Postoperative Bleeding with Adrenosem, Laryngoscope, 55:31 (January) 1955.

2. Peele, J. C.: Adrenosem in the Control of Hemorrhage from the Nose and Throat, A.M.A. Arch. of Otolaryng. 61:450 (April) 1955.

3. Riddle, A. C., Jr.: Adrenosem Salicylate: A Systemic Hemostat, Oral Surg., Oral Med., Oral Path. In press.

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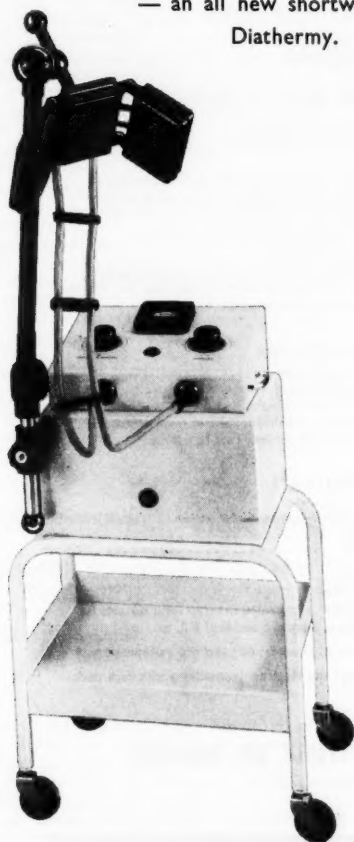
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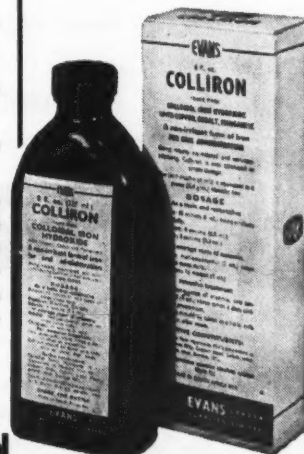
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By L. Schamroth,

M.B., B.Ch. (Rand), M.R.C.P.E., F.R.F.P.S.

University of Witwatersrand and General Hospital,
Johannesburg

Table of Contents**Chapter 1 Basic Principles.**

- 2 Myocardial Death, Injury and Ischaemia.
- 3 Bundle Branch Block.
- 4 Ventricular Hypertrophy.
- 5 Digitalis and Potassium Effect.
- 6 Disorders of Cardiac Rhythm.

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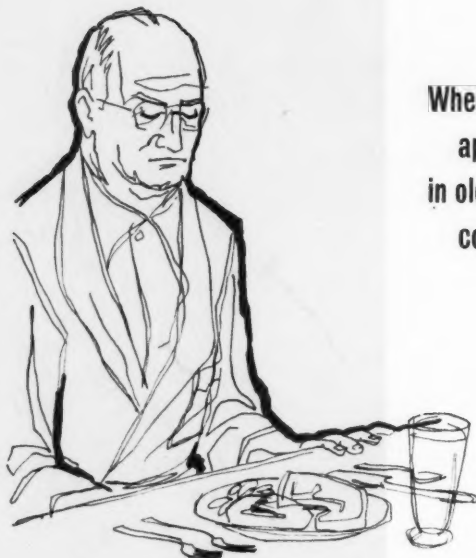
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